CLAIMS

1. A method of preparing a transgenic plant expressing a protein variant having modified immunogenicity as compared to a parent protein, comprising the steps of:

(a) obtaining antibody binding peptide sequences involved in antibody binding,

(b) using the sequences to localize epitope sequences on the primary and/or the 3-dimensional structure of a parent protein,

(c) defining an epitope area including amino acids situated within 5Å from the epitope amino acids constituting the epitope sequence,

(d) changing one or more of the amino acids defining the epitope area of the parent protein by genetic engineering mutations of a DNA sequence encoding the parent protein,

(e) introducing the mutated DNA sequence into a suitable host, culturing the host and expressing the protein variant,

(f) evaluating the immunogenicity of the protein variant using the parent protein as reference,

(g) introducing the mutated DNA sequence into an expression construct and transforming a suitable plant cell with the construct, and

(h) regenerating the plant from the plant cell.

2. The method of claim 1, wherein the sequences of step (a) are obtained by screening a random peptide display package library with antibodies raised against any protein of interest and sequencing the amino acid sequence of the antibody binding peptide, or the DNA sequence encoding the antibody binding peptide.

3. The method of claim 2, wherein antibodies for screening the random peptide display package library are raised against the protein allergen.

4. The method of claim 2, wherein the peptide display package library is a phage display library.

5. The method of claim 1, wherein the antibody binding peptide sequences of step (a) are obtained by screening a library of known peptides related to the primary sequence of any protein of interest, with antibodies raised against the protein of interest.

6. The method of claim 1, wherein epitope patterns are identified by sequence alignment of antibody binding peptide sequences and these epitope patterns are used to guide localization of epitope sequences on the 3-dimensional structure of the parent protein.

7. The method of claim 1, wherein the epitope area of step (c) equals the epitope sequence.

8. The method of claim 1, wherein hot spot amino acids of the parent protein are identified.

9. The method of claim 1, wherein the epitope area is changed by substituting, adding and/or deleting at least one amino acid.

10. The method of claim 1, wherein the epitope sequence is changed by substituting, adding and/or deleting at least one amino acid.

11. The method of claim 1, wherein the hot spot amino acids are changed by substituting, adding and/or deleting at least one amino acid.

12. The method of claims 9, wherein amino acids in the epitope area are changed by substituting and/or inserting at least one amino acid by an amino acid which render the substituted and/or inserted amino acid a target for in vivo posttranslational modification.

13. The method of claim 10, wherein amino acids in the epitope sequence are changed by substituting and/or inserting at least one amino acid by an amino acid which render the substituted and/or inserted amino acid a target for in vivo posttranslational modification.

14. The method of claim 11, wherein the hot spot amino acids are changed by substituting and/or inserting at least one amino acid by an amino acid which render the substituted and/or inserted amino acid a target for in vivo posttranslational modification.

15. The method of claim 9, wherein the amino acid for substitution and/or insertion is selected from the group consisting of K, C, D, E, Q, R and Y.

16. The method of claim 10, wherein the amino acid for substitution and/or insertion is selected from the group consisting of K, C, D, E, Q, R and Y.

17. The method of claim 11, wherein the amino acid for substitution and/or insertion is selected from the group consisting of K, C, D, E, Q, R and Y.

18. The method of claim 1, wherein the immunogenicity is measured by antibody binding assays.

19. The method of claim 1, wherein the protein variant has reduced allergenicity.

20. The method of claim 19, wherein the allergenicity of the protein variant is less than 75% of the allergenicity of the parent protein.

21. The method of claim 20, wherein the allergenicity of the protein variant is less than 50% of the allergenicity of the parent protein.

22. The method of claim 21, wherein the allergenicity of the protein variant is less than 25% of the allergenicity of the parent protein.

23. The method of claim 1, wherein the parent protein is an environmental allergen.

24. The method of claim 23, wherein the parent protein is a food allergen.

25. The method of claim 1, wherein the host cell in step e) is a bacteria, fungal or plant cell.

26. The method of claim 25, wherein if the host in step e) is a bacteria or a fungal cell, the evaluating of the immunogenicity in step f) should be carried out on protein expressed by a plant cell.

27. A transgenic plant and a seed thereof transformed with a nucleotide sequence encoding a protein allergen having modified immunogenicity as compared to a parent protein.

28. The plant of claim 27, wherein the protein allergen is selected from the group consisting of food allergens.

29. The plant of claim 27, wherein the protein allergen is modified by changing the epitope area, epitope sequence or hot spot amino acids by substituting, adding and/or deleting at least one amino acid.

30. The plant of claim 29, wherein amino acids in the epitope area, the epitope sequence or the hot spot amino acids are changed by substituting and/or inserting at least one amino acid by an amino acid which render the substituted and/or inserted amino acid a target for in vivo posttranslational modification.

31. The plant of claim 29, wherein the amino acid for substitution and/or insertion is selected from the group consisting of K, C, D, E, Q, R and Y.

32. A DNA construct comprising a DNA sequence encoding a protein variant having modified immunogenicity as compared to a parent protein.

33. An expression vector comprising a DNA construct of claim 32.

34. A host cell transformed with the expression vector of claim 33.